CARBONYLATION PROCESS

TECHNICAL FIELD

This invention relates to a process for the carbonylation of an unsaturated reactant in the form of a compound having an aliphatic moiety with at least one unsaturated carbon-carbon bond which comprises reacting the unsaturated reactant with carbon monoxide and a nucleophilic co-reactant in the presence of a carbonylation catalyst to produce a product containing a single unit of the unsaturated reactant in its reacted form.

BACKGROUND ART

Carbonylation reactions of unsaturated compounds, such as olefinically or acetylenically unsaturated compounds are well known in the art. The carbonylation of olefins has been described in numerous European patents and patent applications, e.g. EP-A-0495548, EP-A-0227160, EP-A-0495547, EP-A-0489472, EP-A-0282142, EP-A-04489472, EP-A-0106379 and EP-A-0799180. Examples for the carbonylation of acetylenically unsaturated compounds can be found in EP-A-0499329, EP-A-0441447 and WO 9515938.

Depending on the nature of the co-reactant, the said unsaturated compounds can be converted into esters, acids, anhydrides thio-esters and amides, etc. The

carbonylation of olefins with nucleophilic compounds in the presence of a Group VIII metal catalyst has been extensively described in the textbook "New Syntheses with Carbon Monoxide", Ed. J. Falbe (Springer-Verlag 1980). It is believed that the carbonylation reactions proceed under the influence of an active catalyst system containing one or more Group VIII metal cations, in complex coordination with an organic ligand and a suitable anion.

The appropriate organic ligand is usually selected from a mono- or bidentate ligand.

The source of anions is usually a protonic acid. Preference is in particular given to sources of non- or weakly coordinating anions. Since halide anions, in particular a chloride anion, tend to coordinate fairly strongly to palladium (Group VIII metal), the anion is preferably derived from strong acids excluding hydrohalogenic acids.

A major drawback in said carbonylation reactions is the tendency of the ligand, like organophosphines, to react with catalyst intermediates and/or reaction products and/or reagents and/or reaction diluents to form inactive phosphonium salts. For examples see R.P. Tooze et al. *J. Chem. Soc., Dalton Trans.*; (2000); 3441. The subsequent loss in catalyst activity and stability due to reduced concentrations of the stabilising ligand renders these reactions unfavorable from a commercial point of view.

A specific example of such a case is in hydroesterfication reactions (carbonylation reaction of an unsaturated reactant with an alcohol as nucleophilic co-reactant) where the acid promoter (that is the source of the anion) can react with the alcohol (most notably with methanol as the co-reagent) leading to a fraction of the acid being esterified. It is believed that the product of this side reaction can act as a potent alkylating agent which subsequently reacts with the free ligand (most notably triorganophosphine ligands) in solution to form inactive phosphonium salts of the ligands. In this manner, substantial amounts of the anion and ligand are lost from the reaction medium. This leads to lower catalyst activity, and with time to loss of the palladium metal due to plating.

It is generally understood that the use of bidentate ligands will in part reduce the formation of inactive ligand species formed during the course of catalysis due to the substantially lower concentrations of bidentate ligand that is needed to stabilize the metal cations compared to monodentate ligands. Examples of such bidentate ligands in the form of aliphatic diphosphines are disclosed in EP-A-0227160, EP-A-0495547, EP-A-0495548 and WO 9619434.

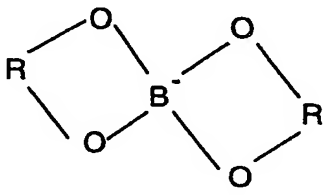
The problem of ligand loss in carbonylation reactions can also be reduced by using a weaker carboxylic acid as a source of anion (also known as a promoter) as disclosed in WO 97/03943. The formation of inactive phosphonium salts was indeed reduced but with subsequent loss in overall catalyst activity when

compared to strong acid promoters like methanesulphonic acid. In order to overcome this problem, the use of sterically hindered carboxylic acids is disclosed in EP-A-0495547. The use of bulky substituents tend to minimize the tendency of the derived anion to coordinate to the metal cation, thereby creating a more active catalyst. However, the weak acids tend to react more readily and irreversibly with a nucleophilic co-reactant than the strong acids, thereby increasing the content of contaminants, making this option less attractive.

EP-A-0121965 describes the co-polymerisation of alkenes and carbon monoxide, in the presence of a carbonylation catalyst comprising a Group VIII metal cation, a bidentate ligand and an acid promoter with a pKa of less than 2. The patent does not disclose any salt formation of ligands in the presence of strong acids like methanesulphonic acid and *p*-toluene sulphonic acid under co-polymerisation conditions. The use of a strong acid promoter that will supply an essentially non-coordinating anion is seen as crucial for the formation of an active carbonylation catalyst. Unfortunately, there seems to be a direct correlation between the use of strong acid promoters like these and an enhancement in salt formation of the ligands in carbonylation reactions of unsaturated reactants to produce a product containing a single unit of the unsaturated reactant in its reacted form.

The use of a certain class of boron containing acid (as a source of anion) serving as a promoter having the general formula (I) is described in EP 039 6268, EP 039 1579, EP 031 5318 and EP 031 4309 and relate specifically to the

preparation of poly-ketones from olefins and carbon monoxide. It is will be appreciated that such poly-ketones include mutiple units of the unsaturated reactant (olefin) in its reacted form. These boron containing promoters are strong enough acids to produce a highly active palladium catalyst.



.....(I)

wherein R is an organic group as defined in these patents.

The inventors have now found that if the anions of the above formula (I) are used instead of the known strong organic acid promoters (for example methanesulphonic acid) in carbonylation reactions of unsaturated reactants to produce a product containing a single unit of the unsaturated reactant in its reacted form, the formation of inactive salts of the free ligand is substantially reduced. These anions were able to activate the appropriate metal cation to form a cationic complex with relatively high catalyst activity. No indication of this advantage is given in the prior art and the results were most unexpected.

DISCLOSURE OF THE INVENTION

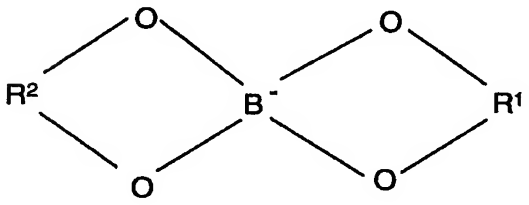
According to the present invention a carbonylation process comprises reacting at least one unsaturated reactant in the form of a compound having an aliphatic

moiety with at least one unsaturated carbon-carbon bond; carbon monoxide; and a nucleophilic co-reactant in the presence of a Group VIII metal catalyst to produce a product containing a single unit of the unsaturated reactant in its reacted form; wherein the catalyst is prepared by the reaction of

i) a source of Group VIII metal;

ii) a ligating compound to coordinate to the Group VIII metal, which ligating compound includes at least one atom selected from phosphorus, arsenic and antimony; and

iii) an anion or a source thereof of general formula (II)



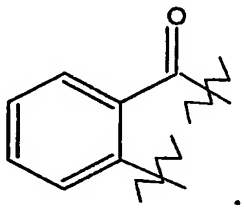
.....(II)

wherein R^1 and R^2 are the same or different and each comprises an organic group.

Anion or source thereof

R^1 and R^2 in formula (II) may each comprise a hydrocarbyl or a heterohydrocarbyl.

In a preferred embodiment of the invention at least one of, but preferably both of R^1 and R^2 comprise an aromatic compound or a heteroaromatic compound. In a preferred embodiment of the invention R^1 and R^2 may independently comprise a compound selected from the group consisting of C_1 to C_6 alkylene; ortho-phenylene; biphenylene; a moiety of the general formula (III); a moiety of general formula (IV)



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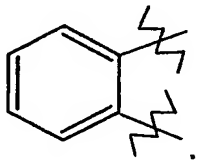

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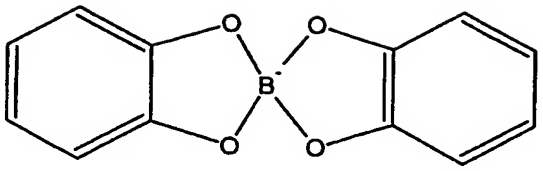
and a substituted derivative of any one of said compounds. The substituted derivative may for example comprise one of the above compounds wherein at least one H is substituted with for example halogen, alkyl, amine, or a nitro moiety. Preferably R^1 and R^2 are the same.

In one embodiment of the invention the anion may comprise the compound (V)



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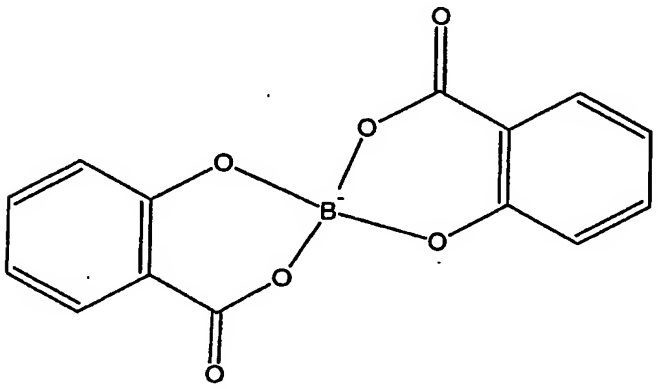
or a substituted derivative thereof. The substituted derivative may for example comprise the above compound wherein at least one H is substituted with for example halogen, alkyl, amine or a nitro moiety.

In another embodiment of the invention the anion may comprise the compound (VI)



.....(VI)

or a substituted derivative thereof. The substituted derivative may for example comprise the above compound wherein at least one H is substituted with for example halogen, alkyl, amine or a nitro moiety.

Preferably the source of the anion is the conjugate acid of the anion.

In one embodiment of the invention the anion or source thereof may be prepared *in situ*. It may be prepared by a condensation reaction between boric acid and a suitable precursor of R^1 and R^2. In the case of compound (V) the precursor of R^1 and R^2 may be catechol. In the case of compound (VI) the precursor of R^1 and R^2 may be salicylic acid.

In another embodiment of the invention the source of the anion may be preformed.

Carbonylation process and co-reactant

In one preferred embodiment of the invention the carbonylation process may be for the preparation of an ester or carboxylic acid. In such a case the nucleophilic co-reactant comprises a source of hydroxyl.

It will be appreciated that in such a case the reaction conditions will be selected in order that esters or carboxylic acids form instead of polyketones. These suitable reaction conditions are well known in the art and may include the use of a monodentate ligand like triphenyl phoshpine; a bindentate ligand like 1,3-bis(di-tertbutylphosphino)propane, or combinations or one or more of these.

In a preferred embodiment of the invention the process may be for preparing esters in which case the nucleophilic co-reactant comprises an alcohol. In such

cases the reaction is known as a hydroesterfication reaction. It is foreseen that any suitable alcohol may be used such as methanol, ethanol, propanol, a diol, a polyhydric alcohol and a phenol, but preferably it comprises methanol.

The ester preferably comprises an aliphatic ester. The ester may comprise a non-branched product and in one preferred embodiment of the invention it comprises methyl propionate. In one preferred embodiment of the invention the process comprises a process for the preparation of methyl propionate wherein the unsaturated reactant comprises ethylene and the alcohol comprises methanol. It will be appreciated that in such a case the methyl propionate contains a single unit of ethyl which is the unsaturated reactant in its reacted form.

Unsaturated reactant

The at least one unsaturated reactant having an aliphatic moiety with at least one unsaturated carbon-carbon bond may comprise an olefinic compound in the form of an olefin or a compound including an olefinic moiety. In a preferred embodiment of the invention the olefinic compound comprises an olefin. However it is foreseen that the olefinic compound may comprise a compound which includes an olefinic moiety which compound may include one or more functional groups such as an ester, a nitrite, an alcohol an ether and an acetol.

The at least one olefin preferably comprises only one olefin, and the olefin may include a single double bond. The olefin may comprise an α-olefin and preferably it comprises ethylene.

Carbon monoxide

The carbon monoxide may be from any suitable source of carbon monoxide.

Catalyst

The Group VIII metal catalyst preferably comprises a palladium catalyst. The catalyst may be fully preformed or partly preformed. For example it is foreseen that a source of palladium may be separately reacted with the ligand to provide a preformed precursor catalyst compound, which is further reacted *in situ* to prepare the active catalyst.

In a preferred embodiment of the invention the palladium catalyst is prepared *in situ.*

It is foreseen that any suitable halide free source of palladium may be used such as salts (organic or inorganic) of palladium e.g. carboxylates and nitrates. In one

embodiment of the invention the source of palladium may comprise palladium acetate.

Although it is foreseen that bidentate ligands may be used, in the preferred embodiment of the invention the ligand comprises a monodentate ligand. The ligating compound may comprise a compound with a group VA central atom for example organophosphine, organoarsine and organostibine. Preferably the ligating compound comprises an organophosphine. In one embodiment of the invention it comprises a compound of general formula (VII)

$$P(R^3\ R^4\ R^5) \text{ ---------- (VII)}$$

wherein R^3, R^4 and R^5 are the same or different and are independently organyl groups.

In one embodiment of the invention the ligating compound comprises PPh_3.

Solvent

The reaction is preferably carried out in a solvent. The solvent may comprise an alcohol, but any other solvent may also be used, especially where water is the co-reactant and acts as a source of hydroxyl.

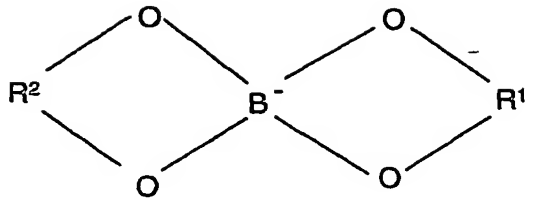
Reaction conditions

The quantity in which the catalyst system is used, is usually not critical and may vary within wide limits. For the preparation of the catalyst systems of the invention, the amount of ligand is generally applied in some excess of the amount of the Group VIII metal, expressed as moles of ligand per mole atom of Group VIII metal. Typically the amount of ligand is selected such that per mole atom of the metal (preferably palladium), in the range of from 1.5 to 500 moles of ligand are present. The amount of the anion source may range from 1 to 500 moles per mole of metal cation.

The process of the present invention is preferably carried out at a temperature from 20°C to 250°C, in particular from 50°C to 150°C and more particularly from 75°C to 120°C.

The process may be conducted under a total pressure of from 5 to 70 bar. Higher pressures may also be used.

According to another aspect of the present invention there is provided the use of an anion or source thereof of general formula (II)



..... (II)

wherein R^1 and R^2 are the same or different and each comprises an organic group;

in a carbonylation process comprising reacting at least one unsaturated reactant in the form of a compound having an aliphatic moiety with at least one unsaturated carbon-carbon bond; carbon monoxide; and a nucleophilic co-reactant in the presence of a Group VIII metal catalyst to produce a product containing a single unit of the unsaturated reactant in its reacted form; wherein the catalyst is prepared by the reaction of

i) a source of Group VIII metal,

ii) a ligating compound to coordinate to the Group VIII metal, which ligating compound includes at least one atom selected from phosphorus, arsenic and antimony; and

iii) the anion or a source thereof of general formula (II);

thereby to reduce the formation of inactive salts of the ligating compound.

The reduction in the formation of inactive salts of the ligating compound may be compared to the same reaction under the same conditions wherein the source of

anion or anion is replaced with a strong organic acid such as methanesulphonic acid.

The invention will now be further described by means of the following non-limiting examples:

Examples

Example 1

A 300ml Hasteloy C autoclave was loaded with 120ml methanol, 0.0538g $Pd(OAc)_2$ (0.239 mmol), 3.147g of PPh_3 (11.99 mmol), 1.483g of $B(OH)_3$ (24 mmol) and 6.629g of salicylic acid (48 mmol). The reactor was then heated to 110°C over a period of 20 minutes while stirring at 1100 rpm. Once the temperature had stabilised the reactor was pressurized with a 1:1 mixture of $CO:C_2H_4$ up to a total pressure of 20 bar. The gas feed was then switched to a 1L ballast vessel (same gas mixture) and reaction progress was followed *via* pressure drop in the ballast vessel. An initial reaction rate of 1020 moles of methyl propionate formed per mole of palladium per hour was observed. After the catalyst performed approximately 1000 catalytic cycles, a sample was taken from the reactor and the amount of methyl triphenylphosphonium sulphonate was quantified with ^{31}P-NMR using $(Bu)_3P(O)$ as internal standard. The ^{31}P-NMR spectrum indicated that no methyl triphenylphosphonium sulphonate (an inactive phosphonium salt) was present in solution. (The small amounts of

triphenylphosphine oxide formed in all reactions were not taken as phosphine decomposition into phosphonium salts. The stoichiometric reduction of palladium acetate with the concomitant oxidation of triphenylphosphine has been reported previously. See C. Amatore et al. *Organometallics.*; (1992); 11; 3009.) GC analysis of the same sample of reaction mixture indicated a 98% selectivity to methyl propionate.

Example 2

Example 1 was repeated with the addition of 6.693g preformed borosalicylic acid to the reaction mixture instead of separate amounts of $B(OH)_3$ and salicylic acid. An initial reaction rate of 886 moles of methyl propionate formed per mole palladium per hour was observed. After the catalyst performed approximately 1000 catalytic cycles, a sample was taken from the reactor and the amount of methyl triphenylphosphonium sulphonate was quantified with ^{31}P-NMR using $(Bu)_3P(O)$ as internal standard. The ^{31}P-NMR spectrum indicated that no methyl triphenylphosphonium sulphonate was present in solution. GC analysis of the same sample of reaction mixture indicated a 98% selectivity to methyl propionate.

In both examples 1 and 2 loss of the ligating compound (triphenylphosphine) was reduced to below 1% (by mass) per gram of ester (methyl propionate) formed.

Example 3 (Comparative)

In a comparative experiment, example 1 was repeated with the addition of 1.557 ml methanesulphonic acid (24 mmol) to the reaction mixture instead of borosalicylic acid. An initial reaction rate of 2144 moles of methyl propionate formed per mole palladium per hour was observed. After the catalyst performed approximately 1000 catalytic cycles, a sample was taken from the reactor and the amount of methyl triphenylphosphonium sulphonate was quantified with ^{31}P-NMR using $(Bu)_3P(O)$ as internal standard. The ^{31}P-NMR spectrum indicated that 72% of the triphenylphosphine was converted into methyl triphenylphosphonium sulphonate in solution. GC analysis of the same sample of reaction mixture indicated a 98% selectivity to methyl propionate.

Example 4 (Comparative)

In a comparative experiment, example 1 was repeated with the addition of 2.616g trifluoroacetic acid (24 mmol) to the reaction mixture instead of borosalicylic acid. An initial reaction rate of 572 moles of methyl propionate formed per mole palladium per hour was observed. After the catalyst performed approximately 1000 catalytic cycles, a sample was taken from the reactor and the amount of methyl triphenylphosphonium sulphonate was quantified with ^{31}P-NMR using $(Bu)_3P(O)$ as internal standard. The ^{31}P-NMR spectrum indicated that 24% of the

triphenylphosphine was converted into methyl triphenylphosphonium sulphonate in solution. GC analysis of the same sample of reaction mixture indicated a 90% selectivity to methyl propionate.

Example 5

Example 1 was repeated with the addition of 8.136g 5-chloro-salicylic acid (24 mmol) instead of 6.629g salicylic acid. An initial reaction rate of 780 moles of methyl propionate formed per mole palladium per hour was observed. After the catalyst performed approximately 1000 catalytic cycles, a sample was taken from the reactor and the amount of methyl triphenylphosphonium sulphonate was quantified with ^{31}P-NMR using $(Bu)_3P(O)$ as internal standard. The ^{31}P-NMR spectrum indicated that 3% of the triphenylphosphine was converted into methyl triphenylphosphonium sulphonate in solution. GC analysis of the same sample of reaction mixture indicated a 98% selectivity to methyl propionate.

It will be appreciated that many variations in detail are possible without thereby departing from the spirit of the invention.